

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date  
1 September 2005 (01.09.2005)

PCT

(10) International Publication Number  
**WO 2005/080552 A1**

(51) International Patent Classification<sup>7</sup>: C12N 5/06,  
15/01, A01K 67/027

(21) International Application Number:  
PCT/EP2005/001897

(22) International Filing Date: 23 February 2005 (23.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
04004062.8 23 February 2004 (23.02.2004) EP

(71) Applicant (for all designated States except US):  
**GSF-FORSCHUNGSZENTRUM FÜR UMWELT UND GESUNDHEIT, GMBH** [DE/DE]; Ingolstädter Landstrasse 1, 85764 Neuherberg (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BUERSTEDDE, Jean-Marie** [DE/DE]; Gunta-Stölzl-Str. 6, 80807 München (DE). **ARAKAWA, Hiroshi** [JP/DE]; Wiegandweg 3, 80937 München (DE).

(74) Agents: **WEBER-QUITZAU, Martin** et al.; Uexküll & Stolberg, Beselerstrasse 4, 22607 Hamburg (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2005/080552 A1

(54) Title: METHODS FOR GENETIC DIVERSIFICATION IN GENE CONVERSION ACTIVE CELLS

(57) **Abstract:** The invention relates to a modified lymphoid cell having gene conversion fully or partially replaced by hypermutation, wherein said cell has no deleterious mutations in genes encoding paralogues and analogues of the RAD51 protein, and wherein said cell is capable of directed and selective genetic diversification of a target nucleic acid by hypermutation or a combination of hypermutation and gene conversion. The invention also relates to a method for diversifying any transgenic target gene in said cell. Preferably, the target gene is integrated into the immunoglobulin light or heavy chain locus by targeted integration.